



ORIGINAL ARTICLE

Impact of public health initiatives on acute coronary syndrome fatality rates in Portugal



Daisy Abreu^{a,b,*}, Paulo Sousa^{a,b,c}, Carlos Matias-Dias^{a,b,c}, Fausto Pinto^{d,e}

^a Escola Nacional de Saúde Pública, Universidade Nova de Lisboa, Lisboa, Portugal

^b Department of Epidemiology of the Instituto Nacional de Saúde Doutor Ricardo Jorge, Lisboa, Portugal

^c Centro de Investigação em Saúde Pública – ENSP-UNL, Lisboa, Portugal

^d Serviço de Cardiologia, Hospital de Santa Maria, Centro Hospitalar Lisboa Norte – EPE, Centro Académico Medicina de Lisboa, Lisboa, Portugal

^e Centro Cardiovascular da Universidade de Lisboa, Lisboa, Portugal

Received 31 December 2018; accepted 26 May 2019

Available online 3 March 2020

KEYWORDS

Public health;
Cardiovascular
health;
Acute coronary
syndrome;
Case-fatality rate

Abstract

Introduction and Objective: Every year cardiovascular disease (CVD) causes 3.9 million deaths in Europe. Portugal has implemented a set of public health policies to tackle CVD mortality: a smoking ban in 2008, a salt reduction regulation in 2010 and the coronary fast-track system (FTS) for acute coronary syndrome (ACS) in 2007. Our goal in this study was to analyze the impact of these three public health policies in reducing case-fatality rates from ACS between 2000 and 2016.

Methods: The impact of these policies on monthly ACS case-fatalities was assessed by creating individual models for each of the initiatives and implementing multiple linear regression analysis, using standard methods for interrupted time series. We also implemented segmented regression analysis to test which year showed a significant difference in the case-fatality slopes. **Results:** Separate modeling showed that the smoking ban ($\beta = -0.861$, $p = 0.050$) and the FTS ($\beta = -1.27$, $p = 0.003$) had an immediate impact after implementation, but did not have a significant impact on ACS trends. The salt reduction regulation did not have a significant impact. For the segmented model, we found significant differences between case-fatality trends before and after 2009, with rates before 2009 showing a steeper decrease.

Conclusions: The smoking ban and the FTS led to an immediate decrease in case-fatality rates; however, after 2009 no major decrease in case-fatality trends was found. Coronary heart disease constitutes an immense public health problem and it remains essential for decision-makers, public health authorities and the cardiology community to keep working to reduce ACS mortality rates.

© 2020 Sociedade Portuguesa de Cardiologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

* Corresponding author.

E-mail address: da.abreu@ensp.unl.pt (D. Abreu).

PALAVRAS-CHAVE

Saúde pública;
Doença
cardiovascular;
Síndrome coronária
aguda;
Letalidade

Impacto das medidas de saúde pública na mortalidade intra-hospitalar por síndrome coronária aguda em Portugal

Resumo

Introdução e objetivo: A doença cardiovascular (DCV) causa 3,9 milhões de mortes na Europa anualmente. Portugal implementou um conjunto de políticas de saúde pública que abordam a mortalidade por DCV, a lei do tabaco em 2008, a lei de redução do sal em 2010 e a via verde coronária (VVC) em 2007. O objetivo deste estudo foi analisar o impacto destas três políticas de saúde na redução das taxas de letalidade por síndrome coronária aguda (SCA) entre 2000 e 2016.

Métodos: O impacto destas políticas na taxa letalidade foi avaliado através da criação de modelos individuais para cada uma das iniciativas. Foi também implementada uma regressão segmentada para testar qual o ano em que houve uma diferença significativa na letalidade.

Resultados: Os modelos individuais mostraram que a lei do tabaco ($\beta=-0,861$, p -valor=0,050) e a VVC ($\beta=-1,27$, p -valor=0,003) tiveram impacto imediato após a sua implementação. A estratégia de redução do sal não teve impacto significativo. Para o modelo segmentado, encontramos diferenças significativas entre as tendências de letalidade antes e depois de 2009, com taxas anteriores a 2009 mostrando uma queda mais acentuada.

Conclusão: A lei do tabaco e a VVC levaram a uma diminuição imediata da taxa de letalidade; no entanto, depois de 2009, não houve redução significativa. A doença coronária constitui um grande problema de saúde pública, é crítico que as autoridades de saúde pública e a comunidade de cardiologia continuem a trabalhar para reduzir as taxas de mortalidade por SCA.

© 2020 Sociedade Portuguesa de Cardiologia. Publicado por Elsevier España, S.L.U. Este é um artigo Open Access sob uma licença CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Every year cardiovascular disease (CVD) causes 3.9 million deaths in Europe and over 1.8 million deaths in the European Union (EU), accounting for 37% of all deaths in the EU.¹ In Portugal and in Europe as a whole, CVD is the leading cause of death.²

Despite recent decreases in mortality rates in many countries, CVD is still responsible for almost half of all deaths in Europe,² and constitutes a major public health challenge in western Europe.³

Of all behavioral components, dietary factors pose the greatest risk for CVD mortality and reduced CVD disability-adjusted life years in the European population. High systolic blood pressure and smoking represent other major risk factors.

Several European countries have implemented measures to tackle CVD mortality, from disease prevention by tackling major risk factors to improvements in disease management and treatment.

As part of this effort, in recent years Portugal has instituted a set of health policies that directly or indirectly tackle CVD mortality, including a smoking ban in 2009, a salt reduction regulation in 2010 and the coronary fast-track system (FTS) for acute coronary syndrome (ACS). The latter policy, which was more directed linked to reducing mortality, was launched in 2000, but was not fully implemented throughout the country until 2007.

There is growing evidence-based data worldwide on the effectiveness of these health policies and public health initiatives; however, reports on the effectiveness of similar

policies in Portugal is scarce. More importantly, there has been no analysis of the cumulative effect of the three major policies recently implemented in Portugal. In the context of increasingly limited resources for health care, investment in population-wide policy strategies needs to show an appropriate return, in this case a decline in CVD mortality. It is therefore important to assess the influence of these policies on observed coronary heart disease (CHD) mortality.

Our aim was thus to analyze the impact of the three health policies implemented in Portugal in reducing ACS case-fatality rates, namely the FTS for primary angioplasty, the smoking ban and the salt reduction regulation, using case-fatality rates from 2000 to 2016.

Methods

Data

Data were obtained from the national Diagnosis-Related Group database, which collects information on all admissions to public hospitals in mainland Portugal, including primary diagnosis, demographic variables such as gender and age, and the geographic region of the admission.⁴ Approval to access the data was previously obtained from the Ministry of Health.

All admissions between 2002 and 2016 of individuals ≥ 20 years of age with a primary diagnosis of ACS, as coded by the International Classification of Diseases, Ninth Revision (ICD-9), were extracted. Codes 410.00-410.xx were used to identify admission diagnoses of acute myocardial infarction

(MI) and 413 codes were used to identify unstable angina. All participants with missing data were excluded from the analysis.

Health policies and public health initiatives

Coronary fast-track system

The FTS was implemented in all regions of Portugal by 2007. We therefore had available for analysis seven years of data before the implementation of the regulation (January 2000–December 2007) and nine years of data after implementation (January 2008–December 2016).

The aim of the FTS was to create a priority system that would facilitate access to clinical, therapeutic and diagnostic resources for ACS patients. Direct admission to the catheterization laboratory for primary angioplasty is essential since the time between symptom onset and treatment in MI is crucial to reducing morbidity and mortality. The system is triggered by patients calling the emergency number (112). The National Institute for Emergency Medicine (INEM) can then initiate diagnosis and treatment earlier by transferring the patient to a hospital unit specializing in ACS treatment.⁵

INEM has the capacity to intervene early, and after clinical diagnosis and electrocardiogram, decides jointly with the Referral Center for Emergency Patients (CODU) on pre-hospital treatment and hospital referral, increasing the likelihood of therapeutic success. CODU contacts the hospital unit to organize the patient's admission and treatment.⁶

Smoking ban

The smoking ban was implemented in January 2008. We therefore had available for analysis six years of data before the implementation of the ban (January 2002–December 2007) and nine years of data after implementation (January 2008–December 2016).

Portugal is a signatory of the World Health Organization (WHO)'s Framework Convention on Tobacco Control,⁷ which led to implementation in January 2008 of the most recent anti-smoking measure, Law no. 37/2007.⁸ This legislation introduced a new framework to protect individuals from passive (second-hand) smoking and to promote smoking reduction and cessation.^{8,9} The law banned smoking in all enclosed public places, including hospitals, public transport, and workplaces. In addition, it established further regulations regarding information provided on tobacco products, their packaging and labeling, as well as further restrictions on advertising.¹⁰

Salt reduction policy

The salt reduction policy was implemented in September 2010. We therefore had available for analysis eight years of data before the implementation of the regulation (January 2002–September 2010) and six years of data after implementation (October 2010–December 2016).

Even small reductions in the prevalence of high blood pressure can lead to major health gains. In view of the importance of these approaches, the WHO created a set of recommendations to reduce dietary salt intake to 5 g/day, in order to prevent chronic disease and improve health.¹¹ In the WHO European Region, 26 out of the 53 member states, including Portugal, have implemented operational

salt reduction policies, including those aimed at reducing salt intake.

Notably, bread accounts for about one-sixth of daily salt intake,^{12,13} with Portugal, Poland and Japan having the highest levels of salt in bread.^{14,15} The policy introduced in Portugal aimed to reduce salt to 1.4 g per 100 g bread. It also mandated clear salt content labeling of packaged products.

Statistical analysis

The main outcome in our study was monthly case-fatality rates, subsequently stratified by age and gender.

ACS case-fatality rates were calculated for each month, using the total number of patients admitted to public hospitals as the denominator and the number of ACS deaths as the numerator.

The impact of the three policies was studied individually, using a binary covariable indicating the start of the policy, as well as a continuous covariable to account for the effect of the policy after its implementation. A segmented multiple linear regression model was implemented to assess changes over time. These models are useful when the relationship between the response and the independent variables is piecewise linear, i.e. represented by two or more straight lines connected at unknown values (breakpoints).¹⁶ In this study, the segmented model was implemented to test for significant changes in case-fatality rates after the introduction of the three policies. The Davies test was used to assess whether the differences between the slopes before and after the breakpoint were significant. The model was fitted in R version 2.5.1 software using the "segmented" library.¹⁷

For all models created, the case-fatality rate was the response variable. Four models were created in total, one for each of the policies and one used subsequently to test which year showed a significant difference in case-fatality rate.

All analyses were stratified by gender and age. Two age categories were used, <65 and ≥65 years. Short-term autocorrelation between monthly estimates was incorporated into the model by applying a first-order autoregressive process to the residuals.

Although we were aware that there might be short-term temporal differences in case-fatality rates, related for example to the day of the week, or weekends vs. weekdays, we did not adjust for this in our models. Other studies have shown a steady reduction in differences between weekends and weekdays in the time of CVD events.¹⁸ There have also been studies showing that after accounting for mode of arrival at the hospital, there was no difference in case-fatality rates between weekdays and weekends.¹⁹

Statistical significance was assessed through p-values, assuming <5% as significant, and 95% confidence intervals (CI) were calculated for each of the regression coefficients. Models were fitted in R software, version 2.5.1.

Results

A total of 20 849 in-hospital deaths from ACS were recorded in mainland Portugal from 2000 to 2016, out of a total of 203 040 admissions for ACS.

Table 1 Results of segmented linear regression analyses for each of the models for the individual policies.

		beta (95% CI) ^a	p
<i>Smoking ban</i>			
Overall	Time of breakpoint	-0.861 (-1.72 to -0.003)	0.051
	Time of breakpoint ^a time interaction	0.013 (-0.002 to 0.028)	0.087
Male	Time of breakpoint	-0.457 (-1.288 to 0.374)	0.283
	Time of breakpoint ^a time interaction	0.013 (-0.002 to 0.027)	0.089
Female	Time of breakpoint	-1.306 (-2.394 to -0.217)	0.020
	Time of breakpoint ^a time interaction	0.019 (0.001 to 0.038)	0.051
Age <65 years	Time of breakpoint	0.141 (-0.362 to 0.645)	0.583
	Time of breakpoint ^a time interaction	0.012 (0.003 to 0.020)	0.009
Age ≥65 years	Time of breakpoint	-1.169 (-2.209 to -0.129)	0.029
	Time of breakpoint ^a time interaction	0.019 (0.001 to 0.037)	0.045
<i>Salt reduction regulation</i>			
Overall	Time of breakpoint	0.421 (-0.488 to 1.295)	0.365
	Time of breakpoint ^a time interaction	0.012 (-0.006 to 0.031)	0.190
Male	Time of breakpoint	0.538 (-0.319 to 1.395)	0.220
	Time of breakpoint ^a time interaction	0.008 (-0.009 to 0.026)	0.341
Female	Time of breakpoint	0.243 (-0.921 to 1.408)	0.683
	Time of breakpoint ^a time interaction	0.023 (0.0001 to 0.046)	0.052
Age <65 years	Time of breakpoint	0.557 (0.061 to 1.053)	0.029
	Time of breakpoint ^a time interaction	0.005 (-0.005 to 0.015)	0.320
Age ≥65 years	Time of breakpoint	0.711 (-0.404 to 1.826)	0.213
	Time of breakpoint ^a time interaction	0.016 (-0.007 to 0.039)	0.170
<i>FTS</i>			
Overall ^a	FTS implemented	-1.270 (-2.101 to -0.436)	0.003
	FTS implemented ^a time interaction	0.005 (-0.011 to 0.020)	0.565
Male ^a	FTS implemented	-1.064 (-1.869 to -0.258)	0.01
	FTS implemented ^a time interaction	0.006 (-0.009 to 0.021)	0.459
Female ^a	FTS implemented	-1.453 (-2.555 to -0.352)	0.01
	FTS implemented ^a time interaction	0.009 (-0.011 to 0.029)	0.372
Age <65 years ^a	FTS implemented	0.184 (-0.302 to 0.669)	0.459
	FTS implemented ^a time interaction	0.011 (0.003 to 0.019)	0.01
Age ≥65 years ^a	FTS implemented	-0.348 (-1.413 to 0.716)	0.521
	FTS implemented ^a time interaction	0.023 (0.004 to 0.041)	0.016

^a All regression models were adjusted for seasonal effects.

CI: confidence interval; FTS: coronary fast-track system.

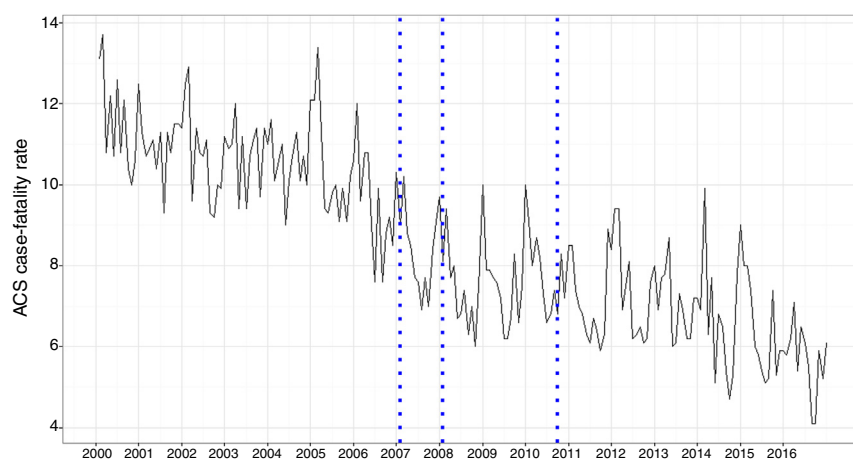


Figure 1 Longitudinal trends for case-fatality rates from acute coronary syndrome (percentages) for January 2000–December 2016. The vertical lines mark when the coronary fast-track system was fully implemented throughout Portugal (2007), the implementation of the smoking ban (2008), and the implementation of the salt reduction regulation (mid-2010). ACS: acute coronary syndrome.

Of the models created individually, one for each policy, the FTS showed an immediate decrease in case fatalities ($\beta=-1.27$, $p=0.003$); however, it did not impact case-fatality trends after 2007, which remained steady. Similarly, the smoking ban resulted in an immediate decrease in case fatalities after its implementation ($\beta=-0.861$, $p=0.05$), but no significant decrease in trends was observed after 2008 (Table 1 and Figure 1).

By contrast, the salt reduction policy did not have any significant effect on case fatalities ($\beta=0.012$, $p=0.189$), or any immediate impact after its implementation ($\beta=0.421$, $p=0.365$; Table 1).

Using a model applying segmented regression, 2009 was identified as a year in which there was a difference in case-fatality rates. Slope trends both before ($\beta=-0.004$; 95% CI -0.005 to -0.004) and after 2009 ($p=0.003$; 95% CI -0.003 to -0.002) showed a decrease; however, after 2009 this was less pronounced ($\beta=0.002$, $p=0.004$) (Table 2).

All four models were stratified for ACS case-fatality rates by gender and age. For females ($\beta=-1.306$, $p=0.020$) and individuals aged ≥ 65 years ($\beta=-1.169$, $p=0.029$), there was a significant decrease in case-fatality rates after the smoking ban. For the FTS, both sexes presented a significant decrease in case-fatality rates; however, there was no difference in trends between age groups (Figure 2).

In the segmented model, the year found to have a differential rate of case fatalities was consistent with the model including all the data (2009). Both trends, before and after 2009, were decreasing, though after 2009 the decrease was not as marked as for the period before 2009, as observed for the model including all the patients.

The differences in case-fatality rates before and after 2009 were higher for women ($\beta=0.003$, $p=0.029$) than for men, and for individuals aged ≥ 65 years ($\beta=0.003$, $p=0.008$; Table 2).

The seasonal pattern was consistent with that reported elsewhere,²⁰ with higher admission rates in winter and lower rates during the summer.

Discussion

In the last 11 years, a set of health policies have been implemented in Portugal to help decrease CVD mortality. The first initiative was the FTS in 2007, followed by the smoking ban in 2008 and the salt reduction regulation in mid-2010.

We created a series of statistical models, four to assess the individual impact of each of the policies, and then one to determine if there was any year during the study that could indicate a difference between trends, suggesting a possible impact of the policies in the country.

The FTS and the smoking ban led to an immediate decrease in case-fatality rates. Previous national and international studies have shown that an FTS, by substantially shortening the time between symptom onset and treatment, directly influences survival. It has been demonstrated that a symptom onset-treatment time of more than 120 min leads to increased in-hospital mortality in an almost linear fashion.^{21–23} However, the FTS in Portugal is mainly aimed at ST-elevation MI, which accounts for around 40% of all ACS, and so it would not be expected to affect non-ST-elevation

MI, meaning that around 60% of ACS patients are not covered by this service.

The relationship between smoking and CVD mortality has been extensively demonstrated. Smoking worsens atherosclerotic alterations, including narrowing the vascular lumen and inducing a hypercoagulable state. Such changes increase the risk of acute thrombosis and thus mortality.²⁴ The results of the current study were very encouraging regarding the smoking ban, as an immediate decrease in case fatalities was found after the ban was implemented. Since the ban targets both smokers and those exposed to second-hand smoke, case-fatality rates should decrease for both groups. Smoking cessation, and even small reductions in consumption, have been linked to decreases in CVD events and in mortality.²⁵

Few studies have analyzed the effect of tobacco control on CVD mortality. Of those available, most focus on how regulations affect hospital admissions²⁶; however, the impact on mortality is equally important. Nevertheless, we are not the first to analyze the impact on mortality. A recent study similarly found a reduction of up to 11% in MI mortality one year after a smoking ban was implemented.²⁷ Another study found a 13% decrease in all-cause mortality, with a decrease of up to 26% in ischemic heart disease (IHD) mortality.

In the current study, we found that 2009 was a breakpoint in our observed trends, which supported the results from the individual models. Up to 2009 the trends were significantly impacted by the policies, leading to a significant decrease in case-fatality rates. After that year, although the trend continued to decrease it was less marked. The impact of the salt regulation in mid-2010 showed a similar effect, with no change in trends after that year. A similar pattern was observed when the impact of this policy on ACS admissions was analyzed.²⁸

We hypothesised that although the salt regulation was an important initiative, it was highly dependent on individual adherence. The way the regulation was implemented may not have produced the desired effect on the population, perhaps due to the low level of health literacy observed in Portugal, and the fact that the policy envisioned a maximum salt content of bread of 1.4 g of salt per 100 g of bread, while other countries set lower limits.

When stratified by gender and age, our results showed that the smoking ban led to an immediate decrease in case-fatality rates for women and individuals aged ≥ 65 years. Although the number of women who smoke has increased in recent years, the number of men smoking was even higher, and their length of time smoking was also greater. As a consequence, men will have increased mortality from CVD, even if they quit smoking or reduce their tobacco consumption. Older people are more vulnerable to exposure to second-hand smoke, and so reducing it could lead to a decrease in case-fatality rates in this group. Our findings were also consistent with another study in which post-ban reductions in IHD mortality were seen in those aged ≥ 65 years, but not in younger subjects.²⁹

Analyzing the impact of the FTS by groups, we found similarly decreasing case-fatality rates for men and women, an effect previously observed in other studies in which the rate of decrease in CHD mortality was similar in both sexes.³⁰ In addition, no immediate change in case-fatality rates was observed after implementation of the FTS for either

Table 2 Results of segmented linear regression analyses in which 2009 was found to be the breakpoint for differences in slopes. Results stratified by gender and age group are also included.

	Pre-breakpoint trend (change per month)	Change in trend in post-breakpoint period compared to pre-breakpoint	Post-breakpoint trend (change per month)
<i>Overall</i>			
Beta ^a	-0.004	0.002	-0.003
95% CI for beta	-0.005 to -0.004	p=0.004	-0.003 to -0.002
<i>Males</i>			
Beta ^a	-0.004	0.002	-0.002
95% CI for beta ^a	-0.004 to -0.003	p=0.022	-0.003 to -0.001
<i>Females</i>			
Beta ^a	-0.007	0.003	-0.004
95% CI for beta	-0.008 to -0.006	p=0.149	-0.006 to -0.002
<i>Age <65 years</i>			
Beta ^a	-0.002	0.001	-0.001
95% CI for beta	-0.003 to -0.001	p=0.154	-0.001 to -0.0002
<i>Age ≥65 years</i>			
Beta ^a	-0.006	0.003	-0.004
95% CI for beta	-0.007 to -0.006	p=0.008	-0.005 to -0.003

^a All regression models were adjusted for seasonal effects.
CI: confidence interval.

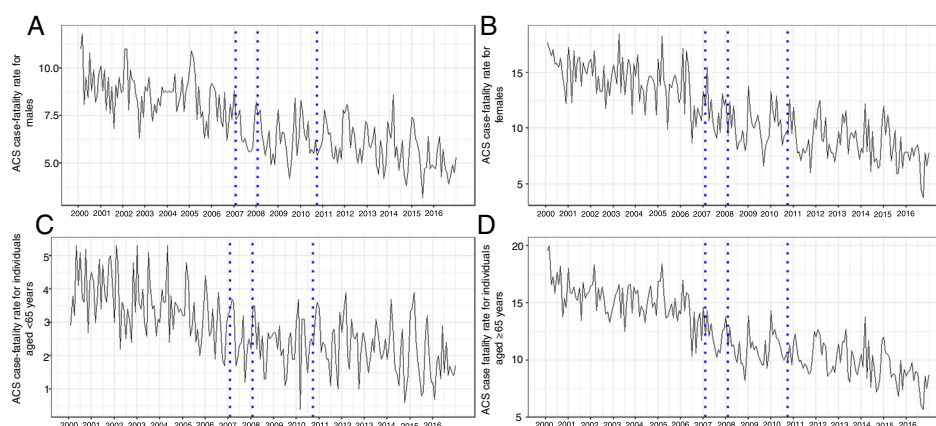


Figure 2 Gender- and age-stratified longitudinal trends for case-fatality rates from acute coronary syndrome (percentage) for January 2000–December 2016. (A) Males; (B) females; (C) individuals aged <65 years; (D) individuals aged ≥65 years. The vertical lines mark the years the policies were implemented. ACS: acute coronary syndrome.

younger or older patients. For both groups, there were significant changes in trend; however, the trends observed were increasing. The prevalence of obesity and diabetes³¹ is rising in Portugal, which could have weakened any reduction in the younger group. This effect has been observed in other studies^{30,32} in which increases in obesity lead to lower reductions in mortality for younger groups. A similar pattern was observed for the older group, which has previously been found in other datasets.³²

Our results for age stratification when using segmented regression showed significant differences between trends before and after 2009, for females and older subjects. As for the non-stratified model, the decrease in trends observed before 2009 was steeper than the decrease observed

afterward. These results were consistent with those observed when studying the smoking ban with age stratification, in which a significant decrease in case-fatality rates was observed for older but not for younger individuals. For the gender stratification, although the FTS analysis showed a significant decrease after 2007 for men, this was an immediate effect and not a trend.

Limitations

As in any ecological study, it is not possible to directly prove any association between policy implementation and the reduction in case-fatality rates from ACS.

One of the strengths of our study is the use of a well-validated and standardized database, enabling easy comparison with other studies in different countries, particularly in other European countries. In addition to the availability of information on gender and age, this enabled us to assess the robustness of our findings among different subgroups. The time-series method is preferred over the simpler pre- and post-proportion comparison method, because it does not take pre-intervention trends into account and also enables corrections to be made for autocorrelation.³³

Conclusions

This study extends the existing literature on the patterns of ACS mortality over time, and assesses whether public health interventions to reduce mortality by ACS were successful. Furthermore, it indicates that to decrease case-fatality rates a multifactorial strategy was needed, rather than a single approach.

Strategies such as the smoking ban and the FTS led to an immediate decrease in case-fatality rates; however, after 2009 no major decreases in ACS trends were found.

Considering that CHD constitutes an immense public health problem,³⁴ it is crucial for different stakeholders, including decision-makers, public health authorities, medical societies and the cardiology community, to keep working together to reduce ACS mortality rates.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

- Wilkins E, Wilson L, Wickramasinghe K, et al. European Cardiovascular Disease Statistics 2017. Brussels: European Heart Network; 2017.
- Nichols M, Townsend N, Scarborough P, et al. Cardiovascular disease in Europe 2014: epidemiological update. *Eur Heart J*. 2014;35:2950–9.
- Karwalajtys T, Kaczorowski J. An integrated approach to preventing cardiovascular disease: community-based approaches, health system initiatives, and public health policy. *Risk Manag Healthc Policy*. 2010;3:39.
- Administração Central do Sistema de Saúde IPA, I.P. Base de Dados Nacional de Grupos de Diagnósticos Homogêneos (GDH); 2011. Available from: [http://portalcodgdh.min-saude.pt/index.php/Base_de_Dados_Nacional_de_Grupos_de_Diagn%C3%B3sticos_Homog%C3%A9neos_\(GDH\)](http://portalcodgdh.min-saude.pt/index.php/Base_de_Dados_Nacional_de_Grupos_de_Diagn%C3%B3sticos_Homog%C3%A9neos_(GDH)) [updated 02.08.11].
- Direção Geral de Saúde. In: Cérebro-Cardiovasculares PNpaD, editor. Rede de Referência de Cardiologia. 2015. Lisboa.
- Soares S. Estudo dos tempos decorridos no atendimento da pessoa com Enfarte Agudo do Miocárdio no Serviço de Urgência. Coimbra: Escola Superior de Enfermagem de Coimbra; 2016.
- Yach D. WHO framework convention on tobacco control. *Lancet*. 2003;361:611.
- Lei n.º 37/2007 de 14 de Agosto, 1.ª Série, n.º 156. 2007.
- Areias Á, Duarte J, Figueiredo J, et al. Asthma and the new anti-smoking legislation. What has changed? *Rev Port Pneumol (Engl Ed)*. 2009;15:27–42.
- Direção Geral de Saúde. Avaliação de impacto da lei do tabaco com foco na equidade; 2014. Lisboa.
- Campbell N, Legowski B, Legetic B, et al. Targets and time-lines for reducing salt in processed food in the Americas. *J Clin Hypertens*. 2014;16:619–23.
- Quilez J, Salas-Salvado J. Salt in bread in Europe: potential benefits of reduction. *Nutr Rev*. 2012;70:666–78.
- Sharp D. Labelling salt in food: if yes, how? *Lancet*. 2004;364:2079–81.
- Castanheira I, Figueiredo C, André C, et al. Sampling of bread for added sodium as determined by flame photometry. *Food Chem*. 2009;113:621–8.
- Appel LJ. ASH position paper: dietary approaches to lower blood pressure. *J Clin Hypertens*. 2009;11:358–68.
- Muggeo VM. Segmented: an R package to fit regression models with broken-line relationships. *R News*. 2008;8:20–5.
- Muggeo VM. Package 'segmented' – regression models with breakpoints/change-points estimation; 2015.
- Balinskaite V, Bottle A, Shaw LJ, et al. Reorganisation of stroke care and impact on mortality in patients admitted during week-ends: a national descriptive study based on administrative data. *BMJ Qual Saf*. 2017, bmjqs-2017-006681.
- Anselmi L, Meacock R, Kristensen SR, et al. Arrival by ambulance explains variation in mortality by time of admission: retrospective study of admissions to hospital following emergency department attendance in England. *BMJ Qual Saf*. 2017;26:613–21.
- Madrigano J, Mittleman MA, Baccarelli A, et al. Temperature, myocardial infarction, and mortality: effect modification by individual and area-level characteristics. *Epidemiology (Camb, MA)*. 2013;24:439.
- Cannon CP, Gibson CM, Lambrew CT, et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA*. 2000;283:2941–7.
- Boersma E, Maas AC, Deckers JW, et al. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet*. 1996;348:771–5.
- Amit G, Cafri C, Gilutz H, et al. Benefit of direct ambulance to coronary care unit admission of acute myocardial infarction patients undergoing primary percutaneous intervention. *Int J Cardiol*. 2007;119:355–8.
- Centers for Disease Control and Prevention (US); National Center for Chronic Disease Prevention and Health Promotion (US); Office on Smoking and Health (US). How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease: a report of the surgeon general. Atlanta, GA: Centers for Disease Control and Prevention (US); 2010.
- Mons U, Müezzinger A, Gellert C, et al. Impact of smoking and smoking cessation on cardiovascular events and mortality among older adults: meta-analysis of individual participant data from prospective cohort studies of the CHANCES consortium. *BMJ*. 2015;350:h1551.
- Abreu D, Sousa P, Matias-Dias C, et al. Longitudinal impact of the smoking ban legislation in acute coronary syndrome admissions. *BioMed Res Int*. 2017;2017.
- Abe TM, Scholz J, de Masi E, et al. Decrease in mortality rate and hospital admissions for acute myocardial infarction after the enactment of the smoking ban law in São Paulo city, Brazil. *Tob Control*. 2017;26:656–62.
- Abreu D, Sousa P, Matias-Dias C, et al. Cardiovascular disease and high blood pressure trend analyses from 2002 to 2016: after the implementation of a salt reduction strategy. *BMC Public Health*. 2018;18:722.
- Stallings-Smith S, Zeka A, Goodman P, et al. Reductions in cardiovascular, cerebrovascular, and respiratory mortality

- following the national Irish smoking ban: interrupted time-series analysis. *PLOS ONE*. 2013;8:e62063.
30. Nichols M, Townsend N, Scarborough P, et al. Trends in age-specific coronary heart disease mortality in the European Union over three decades: 1980–2009. *Eur Heart J*. 2013;34:3017–27.
 31. Marques-Vidal P, Ravasco P, Dias C, et al. Trends of food intake in Portugal, 1987–1999: results from the National Health Surveys. *Eur J Clin Nutr*. 2006;60:1414–22.
 32. Gerber Y, Jacobsen SJ, Frye RL, et al. Secular trends in deaths from cardiovascular diseases: a 25-year community study. *Circulation*. 2006;113:2285–92.
 33. Ma Z-q. Use of interrupted time-series method to evaluate the impact of cigarette excise tax increases in Pennsylvania, 2000–2009. *CDC*. 2013;10.
 34. Wong ND. Epidemiological studies of CHD and the evolution of preventive cardiology. *Nat Rev Cardiol*. 2014;11:276–89.